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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,534	07/31/2003	Matthew M. Winkler	AMBI:065US	4029

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,534	WINKLER ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *64-66 and 69-104* is/are pending in the application.

4a) Of the above claim(s) *74,75 and 102-104* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64-66,69-73 and 76-101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *7/31/03* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action filed on January 18, 2007 has been acknowledged.

Status of the Application

2. Claims 64-66, 69-73, 76-101, are pending. Claim 64 is amended. Claims 74-75, 102-104 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group. Applicants' response to the office action is fully considered. All arguments have been fully considered and thoroughly reviewed, but are deemed persuasive for the reasons that follow. While incorporating the limitations of the canceled claims 105-106, the amendment introduces new limitation ' tag having a 5' end comprising an amplification domain, a 3' end that is complementary to the first target nucleic acid, and an intervening sequence comprising a first differentiating domain, extending the hybridized nucleic acid tags separately for first and second samples and mixing the first and second sample to create a mixture' which are not present in the previously examined claims. Accordingly new combination of rejections is applied to reject newly presented claims. This action is made FINAL necessitated by Amendment.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 64-66, 69-73, 76-84, 86-101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kato et al. (EP 0 870 842) in view of Shuldiner et al. (Gene, Vol. 91, pp. 139-142, 1990).

Kato et al. teach a method of claims 64, for comparing one or more nucleic acid targets within two or more samples comprising:

(a) preparing a sample mixture by a process comprising preparing tagged first and second nucleic acid samples wherein the method comprises preparing tagged first and second nucleic acid samples each tag comprises a differentiation domain (restriction enzyme recognition domain) and amplification domain (primer binding domain) (see page 8, line 1-39, page 10, line 10-57),

(b) mixing tagged first and second samples to create a mixture and performing a first amplification reaction on a first target sample (see page 7, line 30-57, page 8, line 1-57, page 9, line 1-57),

(c) differentiating the first and second amplified nucleic acids present in the first target fraction, if any (see page 9, line 10-20, page 12, line 11-23);

(d) comparing abundance of the first amplified nucleic acid target of said first sample to the abundance of the first nucleic acid target of the said second sample (see page 9, line 20-37, page 12, line 24-40).

With regard to claim 65, Kato et al. teach that the amplification reaction on the first target fraction is performed using a first target-specific primer (see page 4, line 26-30, page 8, line 6).

With regard to claim 66, Kato et al. teach that the method comprises performing a second amplification reaction using a second target specific primer (see page (page 11, line 41-57, page 12, line 1-10).

With regard to claims 69-73, 77, Kato et al. teach that the tags are appended between amplification domain and the target sequence and the method comprises plurality of samples and plurality of tags, wherein the tags are functional equivalent or identical to amplification domain (see page 2, line 25-36, page 10, line 1-57, indicating that the method comprises at least two samples and different adaptor tags having at least one restriction site, which reads on plurality of samples and tags).

With regard to claim 76, 88-92, Kato et al. teach that the differentiation domain comprises an affinity domain, which are labeled (labeled adaptor has affinity to streptavidin-coated para-magnetic beads) (see page 8, line 1-57, page 10, line 1-57).

With regard to claims 78-84, 86-87, Kato et al. teach that the first target fraction is isolated by binding a ligand (adaptor), which is a nucleic acid complementary to a segment of said target and said complementary nucleic acid is used to separate the first target from the

plurality of the nucleic acid targets by binding it to a solid support (paramagnetic beads) (see page 8, line 1-57, page 10, line 1-57).

With regard to claims 93-96, Kato et al. teach that the affinity domain comprises a first detectable signal specific to the first target and a second detectable signal specific to the second target and results in distinguishable detectable signal (see page 12, line 14-35).

With regard to claims 97-98, Kato et al. teach that the differentiating comprises sequencing the amplified nucleic acids and the differentiation domain is a unique size domain (see page 12, line 11-40, page 2, line 35-36).

With regard to claim 99-101, Kato et al. teach that the tags comprise at least one additional domain comprising one or more restriction enzyme domains (see page 2, line 35-36, page 5, line 10-41).

However, Kato et al. did not teach hybridizing a nucleic acid tag comprising 5' amplification domain, 3' end complementary to a target nucleic acid sequence and an intervening sequence comprising a differentiating domain.

Shuldiner et al. teach a method for generating tagged nucleic acid sequences, wherein Shuldiner et al. teach that method comprises hybridizing an oligonucleotide comprising a 5' end unique sequence and 3' end complementary to a region of target nucleic acid and an intervening sequence comprising differentiating domain (see page 139, col. 2, paragraph 1 under experimental and discussion section, page 140, Fig. 1) and extending the hybridized sequence to produce a tagged nucleic acid sequence (see page 140, Fig. 1, page 141, col. 1, paragraphs 1-3).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of comparing one or more nucleic acid targets as

taught by Kato et al. with a step of using an oligonucleotide to tag a target nucleic acid as taught by Shulinder et al. for the purpose of developing a sensitive assay to compare the expression of plurality target nucleic acid. One skilled in the art would be motivated to combine the method as taught by Kato et al. in a manner taught by Shuldiner et al. because Shuldiner explicitly taught the use of an oligonucleotide having 3' complementary target sequence and 5' unique sequence that result in a tagged target nucleic acid sequence to reduce background noise or false positives (see page 141, col. 1, paragraph under conclusion section, col. 2, paragraph 2). An ordinary artisan would have a reasonable expectation of success that inclusion of an oligonucleotide hybridization would result in a sensitive method for tagging target nucleic acids to generate specific extension products comprising only tagged sequences and reducing the background non-specific target nucleic acids. and such modification of the method would be obvious over the cited prior art.

B. Claim 85 rejected under 35 U.S.C. 103(a) as being unpatentable over Kato et al. (EP 0 870 842) in view of Shuldiner et al. (Gene, Vol. 91, pp. 139-142, 1990) as applied to claims 64-66, 69-73, 76-84, 86-101 above, and further in view of Wang (US 6, 004, 755).

Kato et al. teach a method of comparing one or more nucleic acid targets within two or more samples as discussed above in section 3A.

Although Kato teaches the use of a solid support, neither Kato nor Shuldiner et al. specifically teach that the solid support is an array comprising plurality of complementary nucleic acids bound to said array.

Wang teaches a method for quantitative gene expression analysis using a microarray, wherein the array comprises plurality of complementary probe sequences bound to it (see col. 1, line 66-67, col. 2, line 1-10).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of comparing one or more nucleic acid targets as taught by Kato et al. with a step of using an array as taught by Wang for the purpose of developing a sensitive high throughput assay format to compare the expression of plurality target nucleic acid. One skilled in the art would be motivated to combine the method as taught by Kato et al. in a manner taught by Wang by the inclusion of an array bound complementary nucleic acids because Wang explicitly taught the use of a microarray in screening gene expression of plurality of target sequences in a high throughput format and quantitating the genetic profile (see col. 1, line 6-32, line 66-67, col. 2, line 1-10). An ordinary artisan would have a reasonable expectation of success that inclusion of an array bound complementary sequences would result in a high throughput analysis of plurality of targets at a given time reducing the time to perform the method and use of reagents and such modification of the method would be obvious over the cited prior art in the absence of secondary considerations.

Response to arguments:

4. With regard to the objection to the specification, Applicants' amendment and arguments are fully considered and found persuasive. The objection is withdrawn herein in view of the amendment.

5. With regard to the rejection of claims 64-73, 76-84, 86-101, 15-106 under 35 USC 102(b) as being anticipated by Kato et al., Applicants' amendment and arguments are fully considered and

found persuasive. The rejection is withdrawn herein in view of the amendment and new grounds of the rejection.

6. With regard to the rejection of claim 85 under 35 USC 103(a) as being obvious over Kato et al. in view of Wang et al., Applicants' amendment and arguments are fully considered and found persuasive. The rejection is withdrawn herein in view of the amendment and new grounds of the rejection.

7. With regard to the rejection of claims under provisional double patenting, Applicants arguments are fully considered, however the rejection is maintained as long as the scope of the claims remain within the scope of the instant claims or until a terminal disclaimer is submitted.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
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Art Unit 1637

Prabha Chunduru 3/27/07
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